SAMUEL SALZBERG 1939-2000

Dean of the Faculty of Life Sciences 1998-2000

Genes that Regulate Cell Growth and Differentiation

Career Highlights:

- Ph.D. Weizmann Institute of Science, Rehovot 1970
- Research Associate, St. Louis University, Medical School, St. Louis, Mo., USA (Post-doctoral fellow) 1970-1973
- Joined the Department of Life Sciences in 1973 as a Lecturer
- Deputy Head (1985-1986); Head (1986-1988) Department of Life Sciences
- **Dean**, Faculty of Life Sciences (1998-present)
- Member, Grant Judging Committee - Molecular Biology Section, Israel Academy of Sciences 1987
- Visiting Scientist, National Institutes of Health, Bethesda, MD, U.S.A. 1980; Argonne National Laboratory, Argonne, IL. U.S.A. 1989
- **Full Professor** since 1990
- 67 publications. 62 in Refereed Journals: 5 chapters in books
- Supervised 25 students and 5 are currently enrolled.

Research Interests and Goals:

Our Research focuses on genes that regulate cell growth and differentiation. We use myogenic, erythroleukemic and myeloidleukemic cells as models systems. The effect of ectopic expression of double-stranded RNA activated regulatory proteins (primarily PKR and 2-5A synthetase) or the abolishment of specific gene expression in these cells by molecular means is being studied. We study the expression of cell-cycle factors, such as cyclins, Cdks, pRb, p21(waf1),c-myc, E2Fs etc. as well as the expression of specific differentiation markers in transfected cells. Morphological and confocal microscopy analysis is being used. Our preliminary results indicate that ectopic expression of the genes involved in our studies results in the conversion of malignant cells to the normal phenotype.

Previous and Current Research:

In the past, our group was extensively engaged in studies on the antiretroviral effect of interferon (IFN) both in chronic and exogenously infected cells. Numerous basic findings on the subject were published. More recently we concentrated on the antiproliferative effects of IFN, and in the last few years we study the molecular events of cell growth and differentiation, assuming that the the biological effects of IFN are generated via specific genes. PKR and 2-5A synthetase are just an example of such genes

(or their encoded proteins), and in our view, are key elements in the differentiation process.

Future Projects:

Implementation of studies mentioned above *in vivo*. This will include introduction of PKR or 2-5A synthetase encoding genes into leukemic cells followed by injecting the cells to an appropriate host. Generation of transgenic *animals harboring* these genes fused to constitutive promoters will be attempted. Will the animal be more resistant to viral disease? Will the animal be more resistant to development of cancer?

Present Research Group:

- Adi Heller, M.Sc. Lab Technician
- Dalia Hacohen, M.Sc. Lab Technician
- Yosefa Kronfeld, M.Sc. Ph.D. Student
- Tehila Haiman, M.Sc. Ph.D. Student
- Shenhav Cohen, M.Sc. Ph.D. Student
- Shlomit Vilchik, B.Sc. M.Sc. Student
- Michal Bachrach, B.Sc. M.Sc. Student

Selected Publications

1. Salzberg, S., Mandelbaum, M., Zalcberg, M. and Shainberg, A. (1995) Interruption of myogenesis by transforming growth factor β 1 or EGTA inhibits expression and activity of the myogenic-associated (2'-5')oligoadenylate synthetase and p65 kinase. *Exp. Cell Res*. 219: 223-232.
2. **Salzberg, S.**, Heller, A., Zou, J.-P., Collart, F.R. and Huberman, E. (1996) Interferon-independent activation of (2'-5') oligo adenylate synthetase in Friend erythroleukemia cell variants exposed to HMBA. *J. Cell Science* 109: 1517-1526.
3. Yaffe, A., Schwarz, Y., Hacohen, D., Kinar, Y., Nir, U. and **Salzberg, S**. (1996) Inhibition of 2-5A synthetase experession and activity by antisense RNA interferes with its antiviral and antiproliferative effects and induces cell transformation. *Cell Growth Diff.* 7: 969-978.
4. **Salzberg, S.**, Hyman, T., Turm, H., Kinar, Y., Schwartz, Y., Nir, U., Lejbkowicz, F. and Huberman, E. (1997) Ectopic expression of 2-5A synthetase in human myeloid leukemia cells induces cell-growth arrest and facilitates the appearance of a myeloid differentiation marker. *Cancer Res*. **57**: 2732-2740.
5. Kronfeld-Kinar, Y., Vilchik, S., Hyman, T., Lejbkowicz, F. and **Salzberg, S**. (1999) Involvement of PKR in the regulation of myogenesis. *Cell Growth Diff.* (In Press).